Remarks

Applicants elect Group I (claims 1-3, 5, 7-14, 16, 26, 33, and 72-75) directed to a method of inducing apoptosis in a cell by administering an oligonucleotide that antagonizes Notch-1 expression, with traverse.

Claims 1-5, 7-27, 30-33, 59-66, and 72-75 were pending. Due to the restriction requirement, claims 19-21, 57, 59-66 were cancelled without prejudice to prosecution in another application. Claims 7, 25, and 33 were also cancelled due to the amendment to claim 1. Claims 80-86 are added. Therefore, claims 1-5, 8-18, 22-24, 26-27, 30-32, 72-75 and 80-86 are now pending.

Applicants thank Examiner Epps-Ford and her supervisor John LeGuyader for the courtesy of several telephone interviews with Applicants' representative Sheree Lynn Rybak, Ph.D. to clarify the lack unity of invention asserted in the Restriction Requirement. During these conversations, it was concluded that PCT publication WO 94/07474 does *not* teach exposing a cell to both a differentiation inducing agent and an agent that specifically interferes with Notch function or expression, to induce apoptosis in the cell.

In addition, the relevance of Austin *et al.* (*Development*, 121:3637-50, 1995) to the lack of unity of invention of the pending claims was discussed. It was agreed during a telephone conversation between Examiner Epps-Ford and Sheree Lynn Rybak, Ph.D. on August 8, 2003 that Austin *et al.* does *not* teach exposure of a cell to both agents. As a result of this understanding, Applicants' representative agreed to amend claim 1 to clarify that the target cell is exposed to both a differentiation inducing agent and an agent that interferes with Notch function or expression. Examiner Epps-Ford agreed that if claim 1 was amended in this fashion, the lack of unity of invention rejection would be withdrawn because neither PCT publication WO 94/07474 nor Austin *et al.* teach the administration of both agents.

Amendments to the Specification

Page 4 of the specification was amended to correct typographical errors.

Pages 14 and 15 of the specification were amended to remove references to hyperlinks.

Amendments to the Claims

Claim 1 was amended to include the language from claims 7 and 25. Further support for the amendment can be found throughout the specification, for example page 4, lines 18-21; page 5, lines 13-14; page 9, lines 35-36; page 11, lines 13-14; page 28, lines 14-16; page 41, lines 14-16; and page 42, lines 5-7.

Claim 8 was amended to depend from claim 1 due to the cancellation of claim 7.

Claims 11, 12, 17, and 18 were amended to include the language of amended claim 1.

Claim 23 was amended to clarify the claim.

Claim 31 was amended to depend from claim 1, due to the cancellation of claim 25, and to have the claim language correspond to that shown in claim 1.

Claim 32 was amended to depend from claim 18, due to the cancellation of claim 25, and to have the claim language correspond to that shown in claims 1 and 18.

Claims 73-75 were amended to clarify the antecedent basis.

Support for new claims 80-84 can be found throughout the specification, for example page 10, lines 29-32 and page 11, lines 10-11.

Support for new claim 85 can be found throughout the specification, for example page 38, lines 34-36 and page 39, lines 17-18.

Support for new claim 86 can be found throughout the specification, for example in claim 1 and on page 4, lines 21-26; page 5, lines 22-25.

Restriction Requirement

Although Applicants disagree that a lack of unity has been demonstrated, the claims were revised to simplify the issues and better illustrate that these claims involve a common inventive step that establishes unity of invention. Reconsideration of the restriction requirement is requested in view of these amendments.

The pending claims of the present application were restricted into five groups. The Restriction Requirement concluded that the present invention does not correspond to a technical feature that makes a contribution over the prior art in view of PCT publication WO 94/07474. Applicants disagree, and request reconsideration.

Claim 1 has been amended to clarify that is it directed to a method of inducing apoptosis by exposing the target cell to both an agent that induces differentiation and an agent that interferes with Notch function or expression to induce apoptosis in the target cell. The WO 94/07474 publication does not disclose or suggest the claimed method of exposing a target cell to *both* an agent that induces differentiation of the cell *and* an agent that interferes with Notch function or expression thereby inhibiting a cell fate determining function of a Notch protein in the cell. Because the claims of the present application make an inventive step over the prior art of WO 94/07474, a sufficient *prima facie* case has not been made to support the present restriction requirement, and Applicants request that it be withdrawn. In addition, Applicants note that during the international proceeding of the present application, unity of invention was found. Although the U.S. Patent and Trademark Office is not bound by the PCT finding of unity, this is evidence that the claims have been considered by others to define an inventive step that distinguishes the prior art.

Furthermore, it is not possible to restrict the generic claims in the manner requested in the restriction requirement (e.g. Groups I, II and IV) because the generic claims do not recite antibodies or oligonucleotides, and do not recite Notch-1 or Notch-2, but are instead generic to inducing apoptosis by inducing differentiation and inhibiting a cell fate determining function of a Notch protein in a target cell. The use of Notch-1 or Notch-2 antibodies or antisense molecules are only some specific examples of particular embodiments. Therefore, Groups I, II and IV should be examined in the same application. Group I (directed to methods of inducing apoptosis by administering an oligonucleotide that antagonizes Notch-1 expression), Group II (directed to methods of inducing apoptosis by administering an oligonucleotide that antagonizes Notch-2 expression) and Group IV (directed to methods of inducing apoptosis by administering an antibody that antagonizes Notch protein function) are inherently interconnected. The generic independent linking claim distinguishes over the prior art without making the distinction as to

which agent is used to antagonize Notch function, or which Notch function is antagonized, and the claims must be examined as they are written. Therefore, the invention of Groups I, II and IV are not independent or distinct.

In order to perform a thorough search of the prior art relevant to the broadest claim as written, claim 1, which is directed to methods of inducing apoptosis by exposing a target cell to an agent that induces differentiation, and an agent that inhibits a cell fate determining function of a Notch protein, the prior art relevant to the claims of Groups I, II and IV will have to be searched. This is because claim 1 contains no limitation on the agent used to inhibit Notch protein function. Hence, an examination of claim 1 will inherently find references directed to all of Groups I, II, and IV. In addition, claim 1 contains no limitation on the particular Notch protein function inhibited. Hence, an examination of claim 1 will inherently find references directed to all of Groups I and II. Therefore, there is no additional burden on the Examiner to search the claims of Groups I, II and IV. In the absence of any burden on the U.S. Patent and Trademark Office, Groups I, II and IV should be examined in the same application.

If the Examiner has any questions regarding the present response, she is invited to telephone the undersigned.

Respectfully submitted,

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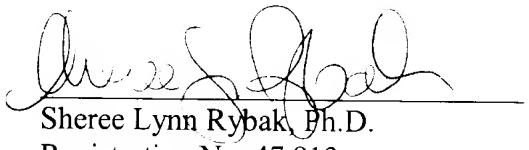
By 
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